CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (canceled)

2. (currently amended) An isolated nucleic acid sequence comprising:

a) a nucleic acid sequence SEQ ID NO:1~~, or variants or portions thereof encoding at least one non-ribosomal peptide synthetase which catalyses at least one step of the biosynthesis of safracins~~; or

b) at least one of the *sacA*, *sacB*, *sacC*, *sacD*, *sacE*, *sacF*, *sacG*, *sacH*, *sacI*, *sacJ*, *orf1*, *orf2*, *orf3* or *orf4* genes; or

c) a nucleic acid sequence encoding any of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins (SEQ ID NO:2-15); or

d) a contiguous portion of SEQ ID NO: 1 encoding a non-ribosomal peptide synthetase which comprises the peptide synthetase core sequences: SGTTG (SEQ ID NO:27), GELCIGG (SEQ ID NO:28), TGD, RIELGEIE (SEQ ID NO:29) and LGGHS (SEQ ID NO:30); or

e) a nucleic acid sequence encoding a non-ribosomal peptide synthetase with at least 95% homology with the polypeptide encoded by the *sacA*, *sacB* or *sacC* genes included in SEQ ID NO: 1 wherein said polypeptide comprises the peptide synthetase core sequences: SGTTG (SEQ ID NO:27), GELCIGG (SEQ ID NO:28), TGD, RIELGEIE (SEQ ID NO:29) and LGGHS(SEQ ID NO:30); or

~~b)~~ f) a nucleic acid sequence which is a full complement ~~fully complementary~~ to the sequence in a), b), c), d) or e).

3. (canceled)

4. (currently amended) The nucleic acid sequence according to claim 2, wherein the nucleic acid sequence comprises:

a) ~~comprises~~ SEQ ID NO:1; or

b) at least one of the *sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ, orf1, orf2, orf3* or *orf4* genes~~, including variants or portions thereof encoding at least one non-ribosomal peptide synthetase which catalyses at least one step of the biosynthesis of safracins~~; or

c) a nucleic acid sequence encoding any of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins (SEQ ID NO:2-15); or

d) a nucleic acid sequence which is a full complement to the sequence in a), b), or c).

5. (canceled)

6. (currently amended) The nucleic acid sequence according to claim 2, wherein the nucleic acid sequence ~~a)~~ encodes for any of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins (SEQ ID NO:2-15)~~, and variants, mutants or portions thereof which catalyse at least one step of the biosynthesis of safracins~~.

7. (currently amended) The nucleic acid sequence according to claim 2, wherein the nucleic acid

sequence ~~a~~) encodes a peptide synthetase, a L-Tyr derivative hydroxylase, a L-Tyr derivative methylase, a L-Tyr O-methylase, a methyl-transferase or a monooxygenase or a safracin resistance protein.

8-10. (canceled)

11. (currently amended) A primer or hybridization probe capable of hybridizing under stringent conditions with a nucleic acid sequence according to claim 2.

12. (currently amended) The primer or hybridization probe according to claim 11 which comprises a sequence of at least 10 nucleotide residues.

13. (currently amended) The primer or hybridization probe according to claim 11 which comprises a sequence between 25 to 60 nucleotide residues.

14-15. (canceled)

16. (withdrawn) A polypeptide encoded by a nucleic acid sequence of any one of claims 2-10.

17. (withdrawn) The polypeptide according to claim 16 which comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2-15.

18. (currently amended) A vector comprising ~~a~~ the nucleic acid sequence of claim 2.

19. (original) The vector according to claim 18 which is an expression vector.

20. (original) The vector according to claim 18 which is a cosmid.

21. (currently amended) A recombinant host cell transformed with one or more nucleic acid sequences according to claim 2.

22. (currently amended) A recombinant host cell comprising a vector of claim 18.

23. (currently amended) The recombinant host cell according to claim 22 wherein the host cell is transformed with an exogenous nucleic acid comprising a gene cluster encoding polypeptides sufficient to direct the synthesis of a safracin.

24. (currently amended) The recombinant host cell according to claim 22 which is a microorganism.

25. (currently amended) The recombinant host cell according to claim 24 which is a bacterium.

26. (previously presented) A recombinant bacterial host cell in which at least a portion of a nucleic acid sequence of claim 2 is disrupted to result in a recombinant host cell that produces altered levels of safracin compound or safracin analogue, relative to a corresponding nonrecombinant bacterial host cell.

27. (original) The recombinant cell of claim 26, wherein the disrupted nucleic acid sequence is endogenous.

28. (withdrawn) A method of producing a safracin compound or safracin analogue comprising fermenting an organism in which the copy number of the gene cluster of claim 1 has been increased.

29. (withdrawn) A method of producing a safracin compound or safracin analogue comprising fermenting an organism in which expression of genes encoding polypeptides sufficient to direct the synthesis of a safracin or safracin analogue has been modulated by manipulation or replacement of one or more genes or sequence responsible for regulating such expression.

30. (withdrawn) A method of producing a safracin compound or safracin analogue comprising contacting a compound that is a substrate for a polypeptide encoded by one or more of the open reading frames of the safracin biosynthesis gene cluster of claim 1 with said polypeptide, wherein the polypeptide chemically modifies the compound.

31. (withdrawn) The method according to claims 28 or 29 wherein the organism is *Pseudomonas* sp.

32. (previously presented) A composition comprising at least one nucleic acid sequence according to claim 2.

33. (withdrawn) A method of combinatorial biosynthesis comprising use of a composition according to claim 32 for the combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins.

34. (withdrawn) Use of P2, P14, analogs and derivatives thereof in combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins.

35-42. (canceled)

43. (currently amended) The nucleic acid according to claim 2 wherein the nucleic acid sequence ~~a)~~ comprises at least one of the *sacABCDEFGH* or *sacIJ* operons.

44. (currently amended) The nucleic acid sequence according to claim 2, wherein the nucleic acid sequence ~~a)~~ comprises at least one of the *sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ, orf1, orf2, orf3* or *orf4* genes.

45. (canceled)

46. (new) The nucleic acid sequence according to claim 44 which comprises *sacA, sacB, sacC, sacD, sacF, sacG, sacH, sacI* and *sacJ* genes.

47. (new) The nucleic acid sequence according to claim 44 which comprises *sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ , orf1, orf2, orf3* and *orf4* genes.

48. (new) The nucleic acid according to claim 46 or 47 wherein *sacI* gene is disrupted.

49. (new) The nucleic acid according to claim 46 or 47 wherein *sacJ* gene is disrupted.

50. (new) The nucleic acid according to claim 46 or 47 wherein *sacI* gene is disrupted and expression of *sacJ* gene has been reconstituted.

51. (new) The nucleic acid according to claim 46 or 47 wherein *sacF* gene and/or *sacG* gene has been disrupted.

52. (new) The nucleic acid sequence according to claim 2 wherein the nucleic acid sequence comprises SEQ ID NO: 1.